Radially Branched Deployment for More Efficient Cell Transplantation at the Scale of the Human Brain.

Journal: Stereotact Funct Neurosurg

Publication Year: 2013

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PubMed link: 23343609

Funding Grants: Development and preclinical testing of new devices for cell transplantation to the brain.

Public Summary:
Background: In preclinical studies, cell transplantation into the brain has shown great promise for the treatment of a wide range of neurological diseases. However, the use of a straight cannula and syringe for cell delivery to the human brain does not approximate cell distribution achieved in animal studies. This technical deficiency may limit the successful clinical translation of cell transplantation. Objective: To develop a stereotactic device that effectively distributes viable cells to the human brain. Our primary aims were to (1) minimize the number of transcortical penetrations required for transplantation, (2) reduce variability in cell dosing and (3) increase cell survival. Methods: We developed a modular cannula system capable of radially branched deployment (RBD) of a cell delivery catheter at variable angles from the longitudinal device axis. We also developed an integrated catheter-plunger system, eliminating the need for a separate syringe delivery mechanism. The RBD prototype was evaluated in vitro and in vivo with subcortical injections into the swine brain. Performance was compared to a 20G straight cannula with dual side ports, a device used in current clinical trials. Results: RBD enabled therapeutic delivery in a precise 'tree-like' pattern branched from a single initial trajectory, thereby facilitating delivery to a volumetrically large target region. RBD could transplant materials in a radial pattern up to 2.0 cm from the initial penetration tract. The novel integrated catheter-plunger system facilitated manual delivery of small and precise volumes of injection (1.36 +/- 0.13 microl per cm of plunger travel). Both dilute and highly concentrated neural precursor cell populations tolerated transit through the device with high viability and unaffected developmental potential. While reflux of infusate along the penetration tract was problematic with the use of the 20G cannula, RBD was resistant to this source of cell dose variability in agarose. RBD enabled radial injections to the swine brain when used with a modern clinical stereotactic system. Conclusions: By increasing the total delivery volume through a single transcortical penetration in agarose models, RBD strategy may provide a new approach for cell transplantation to the human brain. Incorporation of RBD or selected aspects of its design into future clinical trials may increase the likelihood of successful translation of cell-based therapy to the human patient.

Scientific Abstract:
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